

CLAIMS

What is claimed is:

1. An immunogenic composition comprising:
a pharmaceutically acceptable excipient; and
an attenuated bacteria which is resistant to an antimicrobial action of a human defensin.
2. The composition of claim 1, wherein the attenuated bacteria expresses an inhibitor of a human defensin.
3. The composition of claim 2, wherein the human defensin is HD-5.
4. The composition of claim 3, wherein the attenuated bacteria expresses a HD-5 peptide inhibitor selected from the group consisting of HD-5 pro-piece (SEQ ID NO: 5) and pro-HD-5^{Met61} (SEQ ID NO: 6).
5. The composition of claim 1, wherein the attenuated bacteria is selected for resistance to a human defensin by a process selected from the group consisting of spontaneous mutation, transposon mutagenesis and chemical mutagenesis.
6. The composition of claim 1, wherein the attenuated bacteria is *Salmonella enterica* selected from the group consisting of serovars *Typhimurium*, *Enteritidis*, *Typhi*, *Abortus-ovi*, *Abortus-equi*, *Dublin*, *Gallinarum*, and *Pullorum*.
7. The composition of claim 1, wherein the attenuated bacteria is an attenuated pathogenic bacteria selected from the group consisting of *Streptococcus*, *Listeria*, *Staphylococcus*, *Bacillus*, *Coryneforms*, *Enterobacteriaceae*, *Klebsiella*, *Serratia*, *Proteus*, *Shigella* spp., *Haemophilus*, *Non-Typable Haemophilus influenza*, *Bordetella*, *Neisseria meningitidis*, *Pasteurella*, *Treponem*, *E. coli*, *Streptococcus pneumoniae*, *Helicobacter pylori*, *Vibrio cholerae*, *Yersinia* spp., *Porphyromonas gingivalis*, *Legionella pneumophila*, *Staphylococcus aureus*, *Clostridium botulinum*, and *Salmonella enterica*.

8. The composition of claim 1, wherein the bacteria is genetically engineered to express an antigen selected from the group consisting of a human tumor antigen, a viral antigen, a bacterial antigen, a fungal antigen, a parasitic antigen, and an immune disease antigen.
9. The composition of claim 1, wherein the composition is an oral formulation.
10. An immunogenic composition comprising:
 - a pharmaceutically acceptable excipient;
 - an attenuated bacteria; and
 - at least one inhibitor of a human defensin.
11. The immunogenic composition of claim 10, wherein the attenuated bacteria expresses an inhibitor of a human defensin.
12. The immunogenic composition of claim 11, wherein the human defensin is HD-5.
13. The immunogenic composition of claim 10, wherein the inhibitor of human defensin is selected from the group consisting of HD-5 pro-piece (SEQ ID NO: 5), Pro-HD-5^{Met61} (SEQ ID NO: 6), a serpin, alpha 1-proteinase inhibitor, alpha 1-antichymotrypsin and derivatives thereof, alpha 2-macroglobulin and derivatives thereof, a glycosaminoglycan, and dermatan sulfate.
14. The immunogenic composition of claim 10, wherein the attenuated bacteria is *Salmonella enterica* selected from the group consisting of serovars *Typhimurium*, *Enteritidis*, *Typhi*, *Abortus-ovi*, *Abortus-equi*, *Dublin*, *Gallinarum*, and *Pullorum*.
15. The immunogenic composition of claim 10, wherein the attenuated bacteria is an attenuated pathogenic bacteria selected from the group consisting of *Streptococcus*, *Listeria*, *Staphylococcus*, *Bacillus*, *Coryneforms*, *Enterobacteriaceae*, *Klebsiella*, *Serratia*, *Proteus*, *Shigella spp.*, *Haemophilus*, *Non-Typable Haemophilus influenza*, *Bordetella*, *Neisseria meningitidis*, *Pasteurella*, *Treponem*, *E. coli*, *Streptococcus pneumoniae*, *Helicobacter pylori*, *Vibrio cholerae*, *Yersinia spp.*, *Porphyromonas gingivalis*, *Legionella pneumophila*, *Staphylococcus aureus*, *Clostridium botulinum*, and *Salmonella enterica*.

16. The immunogenic composition of claim 10, wherein the bacteria is genetically engineered to express an antigen selected from the group consisting of a human tumor antigen, a viral antigen, a bacterial antigen, a fungal antigen, a parasitic antigen, and an immune disease antigen.
17. The immunogenic composition of claim 10, wherein the bacteria is attenuated by alteration in its Dam gene.
18. The immunogenic composition of claim 17, wherein expression of the Dam gene is increased or decreased relative to wild type.
19. The immunogenic composition of claim 10, wherein the inhibitor of a human defensin inhibits processing of a human defensin pro-peptide.
20. The immunogenic composition of claim 19, wherein the inhibitor of human defensin pro-peptide is selected from the group consisting of a trypsin inhibitor, 4-amidinophelylmethane sulfonyl-fluoride (APMSF), aprotinin and soybean trypsin inhibitor.
21. The immunogenic composition of claim 19, wherein the human defensin is HD-5.
22. The immunogenic composition of claim 20, wherein the inhibitor of human defensin pro-peptide is selected from the group consisting of HD-5 pro-piece (SEQ ID NO: 5) and pro-HD-5^{Met61} (SEQ ID NO: 6).
23. The immunogenic composition of claim 19, wherein the attenuated bacteria is *Salmonella enterica* selected from the group consisting of serovars *Typhimurium*, *Enteritidis*, *Typhi*, *Abortus-ovi*, *Abortus-equi*, *Dublin*, *Gallinarum*, and *Pullorum*.
24. The immunogenic composition of claim 19, wherein the attenuated bacteria is an attenuated pathogenic bacteria selected from the group consisting of *Streptococcus*, *Listeria*, *Staphylococcus*, *Bacillus*, *Coryneforms*, *Enterobacteriaceae*, *Klebsiella*, *Serratia*, *Proteus*, *Shigella spp.*, *Haemophilus*, *Non-Typable Haemophilus influenza*, *Bordetella*, *Neisseria meningitidis*, *Pasteurella*, *Treponem*, *E. coli*, *Streptococcus pneumoniae*, *Helicobacter pylori*, *Vibrio cholerae*, *Yersinia spp.*, *Porphyromonas gingivalis*, *Legionella pneumophila*, *Staphylococcus aureus*, *Clostridium botulinum*, and *Salmonella enterica*.

25. The immunogenic composition of claim 19, wherein the bacteria is genetically engineered to express an antigen selected from the group consisting of a human tumor antigen, a viral antigen, a bacterial antigen, a fungal antigen, a parasitic antigen, and an immune disease antigen.
26. The immunogenic composition of claim 19, wherein the bacteria is attenuated by alteration in its Dam gene.
27. The immunogenic composition of claim 26, wherein expression of the Dam gene is increased or decreased relative to wild type.
28. A bacteria comprising:
- (a) a genetic modification resulting in altered expression of DNA adenine methylase (Dam) relative to the wild type sufficient to attenuate the bacteria's virulence; and
 - (b) a resistance to human-defensin 5 (HD-5) sufficient to allow the bacteria to remain in a patient for a period of time sufficient to generate an immune response.
29. The bacteria of claim 28, wherein the bacteria is selected from the group consisting of *Streptococcus*, *Listeria*, *Staphylococcus*, *Bacillus*, *Coryneforms*, *Enterobacteriaceae*, *Klebsiella*, *Serratia*, *Proteus*, *Shigella spp.*, *Haemophilus*, *Non-Typable Haemophilus influenza*, *Bordetella*, *Neisseria meningitidis*, *Pasteurella*, *Treponema*, *E. coli*, *Streptococcus pneumoniae*, *Helicobacter pylori*, *Vibrio cholerae*, *Yersinia spp.*, *Porphyromonas gingivalis*, *Legionella pneumophila*, *Staphylococcus aureus*, *Clostridium botulinum*, and *Salmonella enterica*.
30. The bacteria of claim 29, wherein the *Salmonella enterica* is chosen from serovars *Typhimurium*, *Enteritidis*, *Typhi*, *Abortus-ovi*, *Abortus-equi*, *Dublin*, *Gallinarum*, and *Pullorum*.
31. The bacteria of claim 28, further comprising a second genetic modification resulting in expression of an antigen selected from the group consisting of a human tumor antigen, a viral antigen, a bacterial antigen, a fungal antigen, a parasitic antigen, and an immune disease antigen.
32. A method of eliciting an immune response in an individual, comprising:
- administering an immunogenic composition to an individual in an amount sufficient to elicit an immune response, wherein the composition comprises a pharmaceutically acceptable carrier, and a live attenuated bacteria resistant to human defensins;

allowing the composition to remain in the individual for a time and under conditions such that the individual generates an immune response.

33. The method of claim 32, wherein the live attenuated bacteria expresses a surface antigen selected from the group consisting of a human tumor antigen, a viral antigen, a bacterial antigen, a fungal antigen, a parasitic antigen, and an immune disease antigen.

34. The method of claim 32, wherein the bacteria is selected from the group consisting of *Streptococcus*, *Listeria*, *Staphylococcus*, *Bacillus*, *Coryneforms*, *Enterobacteriaceae*, *Klebsiella*, *Serratia*, *Proteus*, *Shigella spp.*, *Haemophilus*, *Non-Typable Haemophilus influenza*, *Bordetella*, *Neisseria meningitidis*, *Pasteurella*, *Treponema*, *E. coli*, *Streptococcus pneumoniae*, *Helicobacter pylori*, *Vibrio cholerae*, *Yersinia spp.*, *Porphyromonas gingivalis*, *Legionella pneumophila*, *Staphylococcus aureus*, *Clostridium botulinum*, and *Salmonella enterica*.

35. The method of claim 34, wherein the *Salmonella enterica* is chosen from serovars *Typhimurium*, *Enteritidis*, *Typhi*, *Abortus-ovi*, *Abortus-equi*, *Dublin*, *Gallinarum*, and *Pullorum*.

36. The method of claim 32, wherein the immunogenic composition is an oral formulation.